REMARKS

The Office Action of June 7, 2000 presents the examination of claims 1-10, 14, and 15. Claims 1, 14, and 15 are amended. No new matter is inserted into the application.

Issues under 35 U.S.C. § 112, First Paragraph

Claims 1-10, 14, and 15 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly not being enabled by the instant specification. Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectively requested.

Specifically, the Examiner asserts that the instant specification does not provide "adequate support for claims to methods where sequencing of the complete coding region is critical to the practice of the claimed invention is required." In support of this assertion, the Examiner points to page 8, first full paragraph of the instant specification. Applicants respectfully disagree with the Examiner's interpretation of said paragraph.

The sentence cited by the Examiner reads "...by sequencing at least throughout the part or parts of the p53 gene which encode biologically functional domains...." It is well known in the art that a gene is made up of exons (coding regions) and introns (non-coding regions). At the time of the priority date of the present

invention, the structure of the p53 gene was known. Further, it is evident to one skilled in the art that the exons of the p53 gene encode the biologically functional domains. Thus, contrary to the Examiner's assertions, the cited sentence from the instant specification does indeed contemplate sequencing the complete coding region of human p53.

Nevertheless, in view of the Examiner's remarks, Applicants amend claims 1, 14, and 15 to recite that the nucleotide sequence of the parts of a cancer-related p53 protein which encode biologically functional domains is determined. For these reasons, Applicants respectfully submit that the instant claims comply with 35 U.S.C. § 112, first paragraph, and respectfully request that the instant rejection be withdrawn.

Issues Under 35 U.S.C. § 102

Claim 15 stands rejected under 35 U.S.C. § 102(e) for allegedly being anticipated by Diamandis '283 (U.S. 5,552,283). Applicants respectfully traverse. Reconsideration of the claim and withdrawal of the instant rejection are requested.

Claim 15, as amended, provides for a method to predict the development of neoplasia, by analyzing the entire p53 coding regions and then classifying the neoplasia into different subgroups depending on the presence or absence of a mutation, wherein the

classification alone allows for prognosticating the development of the neoplasia. In contrast, Diamandis '283 fails to disclose a method wherein (1) the entire p53 coding region is analyzed for mutations, and (2) classification based upon mutation in the sequence alone is sufficient to carry out the method. Specifically, Diamandis '280 uses at least a three step hierarchy approach for screening p53 mutations. Specifically, immunochemistry, fragment analysis by PCR, and DNA sequencing are all required to carry out the method disclosed by Diamandis '280.

DNA sequencing is described in Column 7, of Diamandis '283. First, only those exons wherein mutations are likely to occur are sequenced. The resulting sequence data is then analyzed for mutations. If no mutations are found, more exons are sequenced in later reactions. The resulting second set of sequence data is then analyzed for the presence of mutations. These steps are repeated until a mutation is found. In contrast to the present invention, the concept of sequencing the entire coding region of the gene at once in one stage is not taught in the disclosure. Also in stark contrast to the present invention, if one mutation is found in the first sequencing reaction, then other sequencing reactions are presumably not performed. Therefore in cases where there is more than one mutation, only the first mutation would be found and may give incomplete data upon which to base the clinical judgement. In

the present invention, however, all mutations in the coding regions will be found.

Further, Diamandis '283 fails to disclose the present classification system. The Examiner only rejects claim 15 because, "Diamandis clearly teach that both genomic and cDNA sequence of p53 have been sequenced in methods to analyze p53 mutations." The Examiner makes no mention as to where in Diamandis '283 the present classification system is disclosed. According to MPEP 2131, "TO ANTICIPATE A CLAIM, THE REFERENCE MUST TEACH EVERY ELEMENT OF THE CLAIM." "A claim is anticipated only if each and every element as set forth in the claim is found, ether expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2USPQ2d 1051, 1053 (Fed. Cir. 1987). Diamandis '283 simply fails to disclose, explicitly or implicitly, the present classification system. Thus, Diamandis '283 fails to teach every element of claim 15.

In summary, Diamandis '283 fails to disclose a method wherein the entire p53 coding region is analyzed for mutations, and wherein classification based upon mutation in the sequence alone is sufficient to predict neoplasia. For these reasons, Diamandis '283 fails to anticipate the present invention. Applicants respectfully request that the instant rejection be withdrawn.

Issues Under 35 U.S.C. § 103

Claims 1-10, and 14 stand rejected under 35 U.S.C. § 103(a) for allegedly being unpatentable over Elledge et al. (Breast Cancer Res. Treat. 27:95-102, 1993) and Callahan (J. Natl. Cancer Institute, 84:826-827, 1992) in view of Diamandis '283 (U.S. 5,552,283). Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are requested.

The Examiner acknowledges that "Elledge et al. and Callahan et al. differ from the present invention in that they do not detect p53 mutations by sequencing the entire coding region of the gene." Thus, the Examiner relies on Diamandis '283 to make up for the deficiencies of Elledge et al. and Callahan et al. However, the Examiner has improperly made an obvious rejection based upon a combination of these three references.

Specifically, the Examiner must consider the prior art as a whole, including portions that lead away from the claimed invention (MPEP 2141.02). The disclosure of Diamandis '283, as a whole, teaches away from the present invention. In column 2, lines 23-26, Diamandis states, "These rapid DNA-based techniques have used to detect mutations, but because they are so labor intensive, that large scale screening tests are impractical." Continuing at column 2, line 28 onwards, "Thus, the existing methods of diagnosis have

been frustratingly unsatisfactory. Researchers have used either immunoassay or DNA analytical methods...". Line 31, "Sequencing is expensive and so it may be desirable to use a sub-hierarchy within this level to reduce the likelihood of having to sequence all the exons." These statements clearly teach away from the present invention. At line 61, Diamandis '283 discloses, "Alternatively, the user may choose to test all exons simultaneously at once." However, this statement refers to PCR rather than sequencing, and therefore this statement cannot be applied to the present invention. Thus, the teachings of Diamandis '283 cited by the Examiner in support of the obviousness rejection cannot be sustained when even Diamandis '283 clearly proclaims that they are not satisfactory.

Overall, the present invention possesses significant patentable features that the cited prior art references do not possess. Furthermore, Applicants submit the instant claims are fully in compliance with 35 U.S.C. § 112, first paragraph. All of the present claims define patentable subject matter such that this application should be placed into condition for allowance. Favorable action on the merits of the present application is thereby requested.

If there are any minor matters precluding allowance of the present application which may be resolved by a telephone

discussion, the Examiner is respectfully requested to contact Kristi L. Rupert, Ph.D. (Reg. No. 45,702) at (703) 205-8000.

Pursuant to 37 C.F.R. 1.17 and 1.136(a), the Applicants respectfully petitions for a one (1) month extension of time for filing a response in connection with the present application, and the required fee of $110.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §1.16 or under 37 C.F.R. §1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By _____

Gerald M. Murphy
Reg. No. 28,977

P.O. Box 747
Falls Church, VA 22040-0747
(703) 205-8000

GMM/KLR:law